

REMARKS

Claims 1-21 are in this application and have been examined. Claims 1-3 have been amended to recite non-human, non-primate mammals; inherent support is found at page 3, where the list of animals includes a variety of animals, primates and nonprimates. The amendment related to the activation is supported by as-filed Examples 3 and 4. Claims 5 has been amended for improved clarity, and claim 7 has been amended to correct inadvertent typographical errors. None of the amendments made herein constitutes the addition of new matter.

The Requirement for Restriction

The Patent Office has stated that the application contains claims directed to more than one species of the claimed invention. The Patent Office required election of a single specific nonhuman animal and a specific species in claim 21, a specific method of enucleation (see claims 6-12), and a specific method of nuclear transfer (see claims 13-18).

In the current Office Action, the Patent Office has now indicated that the requirement for election of species has been withdrawn.

The Information Disclosure Statement

The Examiner has indicated that the references listed on the Form 1449 have been considered, as well as those references listed on the Form 892.

Applicants respectfully note that the list of references within the Specification was meant to be a bibliography rather than a list of references which all were deemed relevant to patentability. Applicants provided the references believed pertinent to patentability as part of the Information Disclosure with Form 1449.

The Rejections under 35 USC 112, first paragraph

Claims 1-19 have been rejected under 35 USC 112, first paragraph, as the Specification enables non-primate mammals by methods of nuclear transfer but does not reasonably provide enablement for any non-human animals. Applicants respectfully traverse this rejection.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended the claims so as to be limited to nonhuman, non-primate mammals. This limitation is inherently supported by the as-filed application at page 2, where "non-human animals" is recited, and at page 3, where "bovines, equines, ovines, caprines, felines, canines, rodents, and other animals in which implantation of embryos is known to the art" is recited.

In view of the amendments to the claims and the statements above, withdrawal of the rejection under 35 USC 112, first paragraph, is respectfully requested.

The Rejections under 35 U.S.C. 102

Claims 1-6, 14 and 19 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Sato et al. (Human Cell 13:197-202, 2000). Applicants respectfully traverse this rejection.

The Examiner advised the undersigned of the correct citation and provided the reference on September 7, 2006. His help is appreciated.

The cited Sato reference is said to teach that mouse ES cells were known as the filing date and provides evidence that methods of nuclear transfer can be used to generate a viable fetus. The Sato reference is said to further disclose that ES cells can be manipulated to contain a transgene, with proof of principle that they can successfully

serve as a donor to produce a fetus and can serve in conjunction with methods known to the art.

It is not clear that the Sato reference describes successful production of transgenic animals through nuclear transfer. There appears to be no teaching of any maturation of the oocytes harvested from mice in the Sato reference. The oocytes were said to be mice treated so as to effect superovulation, and the harvested oocytes were treated with hyaluronidase to remove cumulus cells.

Applicants respectfully submit that the cited Sato reference does not teach the use of zygotes as the recipient cytoplasm (after enucleation). Sato makes no teaching or suggestion of the activation of oocytes after enucleation. Claim 1 has been amended to specify that the oocyte is activated after enucleation. This aspect is new in the present invention as now claimed. These limitations are supported by the as-filed application in Examples 3 and 4.

Moreover, the Sato reference does not appear to teach that the nucleus which is transferred has been genetically modified to contain heterologous DNA, as is claimed in claim 5 in the present application.

Accordingly, Applicants respectfully submit that the reference does not teach all the limitations of the present invention, there is no anticipation of the invention as claimed by the cited Sato reference, and the rejection under 35 U.S.C. 102(b) must be withdrawn.

The Rejections under 35 U.S.C. 103

The Examiner has noted that this application names joint inventors. Applicants confirm that both inventors were obligated to assign the invention to a common

assignee, The Board of Trustees of the University of Illinois. An assignment has been recorded for this application.

Claims 1-21 have been rejected under 35 U.S.C. 103 as allegedly obvious over Wilmut et al. (1997), Campbell et al. (1997) and Wheeler (1994) (sic). Applicants respectfully traverse this rejection.

The Patent Office has stated that the cited Wilmut and Campbell references teach methods of nuclear transfer and in particular, that totipotent cells can be used to generate viable embryos that can be implanted into pseudo pregnant females to carry those embryos to term. The Wheeler reference teaches that porcine totipotent ES cells existed and could be isolated. Wheeler is further said to teach that similar to mouse ES cells, the porcine ES cells could be used in the generation of transgenic swine. The Examiner has concluded that it would have been obvious at the time the invention was made to use the porcine ES cells taught by Wheeler with the nuclear transfer methods generally disclosed by Wilmut and Campbell in that it would have been obvious to substitute the use of ES cells because they allow continued proliferation and the ability to practice homologous recombination to affect an endogenous gene. The methods of ES manipulation are said to be routine and there allegedly would have been a reasonable probability of success to practice the methods of nuclear transfer with porcine ES cells.

The cited Campbell (1997) reference teaches the desirability of making transgenic animals and discusses certain aspects of suitable cells to serve as either nuclear donors or recipient cells. However, this reference also discusses a number of problems and potential problems encountered in the making of transgenic animals by nuclear transfer. Thus, this cited reference speaks to the difficulties in this technology and would appear to militate against a reasonable likelihood of success in the claimed

invention, as is required for a proper rejection for obviousness; see In re O'Farrell, 7 U.S.P.Q. 2d 1673, C.A.F.C., 1988.

The Wilmut reference teaches (at page 813) that embryos were collected from ewes between 28 and 33 hrs after injecting gonadotropin-releasing hormone, and enucleated as soon as possible. Within 2-6 hrs after collection, the fusion of the nucleus donor cell with the oocyte and activation of the oocyte was accomplished simultaneously by electrical pulsing. By contrast, the claims of the present application require that enucleation of the oocytes take place **after** activation. Then the nucleus of interest is introduced into the enucleated activated oocyte. The cited Wilmut reference does not demonstrate any genetic modification of the nucleus prior to nuclear transfer. In addition, the cited Wilmut reference teaches the use of fetal and adult differentiated cells (somatic cells) as nuclear donors, rather than embryonic stem cells as taught and claimed in the present application. ES cells are very different from somatic cells in that they remain mostly undifferentiated. The undifferentiated nature of the ES cells is important, and the totipotency of a somatic cell is not necessarily the same as the totipotency of an ES cell.

The cited Wheeler reference (1994, per telephone conference with Examiner Woitach) teaches the desirability of producing transgenic animals, but neither sets forth all the claimed steps nor does it set forth enabling teachings for achieving the method as claimed. The cited Wheeler reference teaches the production of chimeric embryos with genetic contributions of the two parents distinguished visually on the basis of coat color. Embryos were said to have been injected with cultured embryonic stem cells, but there does not appear to be any disclosure that oocytes were matured, enucleated and heterologous nuclei then introduced. The methods described produce an animal in which there are cells with different genomes, not an animal in which there is genomic homogeneity. There is no demonstration of nuclear transfer. Thus, Wheeler does not

provide any reasonable probability of success in making transgenic animals using nuclear transfer technology.

The three cited references do not provide sufficient teachings to arrive at the claimed invention. At most they provide an invitation to experiment, but they do not point the way to success in the present invention as claimed.

Because of the problems discussed in the cited references, these references provide, at most, an invitation to experiment. These references do not convey the requisite reasonable probability of success (see, e.g., *In re O'Farrell*, 7 USPQ2d 1673, CAFC 1988) for there to be a proper rejection for obviousness. At most, the cited references, alone or in combination, provide an invitation to experiment.

Accordingly, the invention as claimed is not *prima facie* obvious over the cited references, and the rejection should be withdrawn.

Conclusion

Applicants respectfully submit that the pending claims are in condition for allowance and early notification thereof is requested.

If, in the interest of expediting prosecution, the Examiner has questions or comments, he is invited to telephone the undersigned at the indicated telephone number.

This response is accompanied by a Petition for Extension of Time (three months) and a charge to Deposit Account 07-1969 in the amount of \$510 as required by 37 C.F.R. 1.17 has been authorized. It is believed that the present submission does not necessitate an additional extension of time or the payment of any further fees under 37

Appl. No. 10/632,118
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C.F.R. 1.16-1.17. If this is incorrect, however, please consider this response to include the petition for the time necessary for a timely response and charge any deficiency or credit any overpayment in fees pursuant to the foregoing Rules to Deposit Account No. 07-1969.

Respectfully submitted,

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